IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: P. A. Billing-Medel, *et al.*

Serial No.: 09/049,696

Filed: March 27, 1998

For: REAGENTS AND METHODS USEFUL FOR DETECTING DISEASES OF THE GASTROINTESTINAL TRACT

Examiner: J. Kerr

Group Art Unit: 1633

Case No.: 6067.US.P1

Date: November 1, 2000

CERTIFICATE OF MAILING (37 CFR 1.8 (a))

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the:

Assistant Commissioner for Patents
Washington, D.C. 20231, on:

Date of Deposit: November 13, 2000

Wanda C. Smith
Wanda E. Smith

DECLARATION OF PAULA N. FRIEDMAN Ph.D.

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

1. I am one skilled in the art of cancer diagnostics. I have a Ph.D. in Molecular Biology from Columbia University as well as an M.A. and a M. Phil. in Molecular Biology also from Columbia University. I further have a B.A. in Biology from Dartmouth College.

2. I was a Postdoctoral Fellow in the Laboratory of Dr. Clay Siegall at the Pharmaceutical Research Institute Bristol–Myers Squibb and an Assistant Pharmacologist, Dept. of Clinical Immunology & Biol. Therapy at the MD Anderson Cancer Center.

3. I have nine years of research and development experience in the cancer diagnostic industry. Much of my work has involved the discovery and validation of novel cancer markers to improve the accuracy of diagnosing the onset of cancer. In fact, I am a named inventor of several U.S. Patents, all of which are related to the field of cancer diagnostics.

4. I also have authored numerous journal articles relating to cancer pathology, detection, and metastasis (see Attachment I).

5. I am one of the named inventors of the aforementioned application.

6. I have read and am familiar with the Patent Office Action dated July 6, 2000 and utility rejection under 35 U.S.C. 101 applied against the present application.

7. I have reviewed the data illustrating CEA and PSA tissue specificity generated using the Incyte Lifeseq Gold database (Attachment II), the same database utilized to generate Example 1 in the instant application.

8. CEA is a tissue-specific marker that has been shown to be highly expressed in the GI tract. As evidenced by Attachment II, 61 out of 148 GI libraries express CEA whereas only 27 out of 1,144 other, non-GI tract libraries express this gene. Therefore, CEA is expressed approximately 17 times more in GI tissue when compared to the rest of the body.

9. Similarly, PSA is a tissue-specific marker that has been shown to be highly expressed in the prostate. As evidenced by Attachment II, 65 out of 79 prostate libraries (classified as male genitalia) express PSA whereas only 22 out of 1213 other, non-prostate libraries express this gene. Therefore, PSA is expressed approximately 45 times more in prostate when compared to the rest of the body. Further, the PSA gene product is utilized in screening, prognosis, and monitoring prostate cancer patients by oncologists and it is recommended that all men over the age of 40 be tested yearly with a PSA assay.

10. To those skilled in the art, such as myself, PSA and CEA are well known tumor markers, which indicate cancer of the prostate (PSA) and gastrointestinal (GI) tract (CEA) when the respective gene product is found in the blood sample of a patient.

11. As shown in the instant specification, (Example 1, p.52, starting on line 5) CS194 is 104 times more abundant in GI-tract tissue than non-GI tissue. This substantial expression is approximately 2.3 times more than the expression of PSA in the prostate and approximately 6 times more than the expression of CEA in the colon.

12. Clearly, CS194 is characteristic of a tissue specific marker and able to act as a cancer diagnostic, as evidenced by the above data which shows even greater tissue specificity than that of the cancer markers CEA and PSA.

13. Tissue-specific markers such as PSA and CEA are the most diagnostic tools in early oncology detection and are used on a daily basis.

14. Based on the statistics in the Incyte database, CS194 is clearly a GI specific marker and, therefore, its use as a GI tract cancer marker is unquestionable.

15. I hereby declare that all statements made herein are of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that the statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States code and such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Paula N. Friedman, Ph.D.

11/13/00
Date